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EXAMINER	
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ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/721,144	HARIRI, ROBERT J.	
	Examiner	Art Unit	
	Laura McGillem	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-9,12-13,15-18,20-23,31-32,34-37 and 50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9,12,13,15-18,20-23,31,32,34-37 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/10/06,5/5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/15/2006 has been entered.

It is noted that Claims 1, 18, 31, 34 and 50 have been amended and claim 7 has been cancelled in the amendment filed 4/05/2006. Claims 1-6, 8-9, 12-13, 15-18, 20-23, 31-32, 34-37 and 50 are under examination.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 4/10/2006 and 5/5/2006 were considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8-9, 12-13, 15-17 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 50 are vague and indefinite because they recite the phrase "the contents of said unit being known" and the metes and bounds of "known" are not clear, because it is not clear who is required to know the contents of the unit in order to meet the limitations of the claim.

Claims 2-6, 8-9, 12-13, 15-17 are indefinite insofar as they depend from claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 8, 12, 15-18, 20-23, 31-32, 34-35 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Pykett et al (U.S Patent No. 6,548,299, filed 5/18/2000.

Pykett et al teach a population of cells comprising hematopoietic cells, including CD34+ cells, obtained from blood products. Pykett et al teach that the cells can be used to supplement or replenish a patient's hematopoietic progenitor cell population (see column 19, lines 12-25, for example), which reads on a cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells. Pykett et al teach embodiments wherein the hematopoietic cells are pluripotent or multipotent cells and may obtained

from bone marrow, peripheral blood, umbilical cord blood, placental blood, fetal liver and lymphoid soft tissue (see column 3, lines 37-50). Pykett et al teach that the blood products can be fractionated or enriched. For example, mature differentiated cells can be selected against or CD34+ cells can be selected from the population of cells in the blood product by using paramagnetic anti-CD34 beads (see column 12, lines 31-50, for example).

Specifically, Pykett et al teach that five to ten milliliters of blood were extracted from an umbilical cord prior to infant delivery. After delivery, the placenta was removed and blood contained in the placenta was collected. Pykett et al teach that the cord blood and placenta blood were mixed together before processing (see column 31, lines 10-25, in particular), which reads on cells from a plurality of sources and wherein one source is fetal cord blood or post-partum placenta. Pykett et al teach that the blood was centrifuged to separate mononuclear cells and then remaining erythrocytes were lysed, which reads on exclusion of at least one type of cell from the unit. The remaining number of viable cells was determined by trypan blue exclusion. Pykett et al also teach that human CD34+ progenitor cells were extracted from human fetal thymus. Pykett et al teach that CD34+ cells were isolated using a CD34 progenitor cell selection system comprising mixing the cell sample with anti-human CD34 beads so that cells not bound to the paramagnetic beads could be aspirated away (see column 31, lines 10-40, for example). Pykett et al teach an embodiment in which five thousand CD34+ cells are co-cultured with thymic stromal cells and after 7 days, the CD34+ were harvested. Subsequently, the harvested cells were counted, assessed for viability and the

presence of CD34 was checked using anti-CD34 antibodies in flow cytometry analysis (see column 33, lines 10-60, in particular), which reads on the contents of the unit being known with respect to the numbers and identities of at least some of the plurality of cells, where the identities reflect the presence of absence of at least one antigenic determinant (e.g. CD34+), and also selection of the plurality of potent cells to render the unit suitable for therapy for an indicated disease or condition such as a patient with an immunodeficiency (see column 9, lines 20-30 and column 19, lines 12-20, for example). Pykett et al teach that further immunomagnetic methods, using an antibody to the stem cell antigen AC133, were used to select for an immature phenotype of progenitor cells (see column 32, lines 37-59, in particular), which reads on a AC133 as a second preselected type of cell for the hematopoietic population. The cell preparation taught by Pykett et al reads on a cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells comprising cells obtained from umbilical cord blood and cells from a postpartum placenta wherein at least one type of cell has been removed from the unit (i.e. erythrocytes).

Since the culture taught by Pykett et al started with five thousand CD34+ before expansion, absent evidence to the contrary, after harvest there would be at least about one hundred CD34+ cells. The cell preparation taught by Pykett et al is obtained by separating CD34+ cells from the blood products. One of skill in the art would recognized that blood contains many cell types (erythrocytes, granulocytes, agranulocytes and platelets). If CD34+ cells are separated from the original blood sample, than many or a plurality of cell types have been removed from the unit. Therefore, Pykett et al teach a

cytotherapeutic unit comprising cells from a mixture of cord blood or postpartum placenta wherein a plurality of cells have been removed from the unit.

Pykett et al teach that the cells can be co-cultured with lymphoreticular stromal cells on a biocompatible matrix obtained from lymphoid tissue in order to expand and direct differentiation of the hematopoietic cells (see column 12, 53-67 lines and column 13, lines 1-11). Pykett et al teach that the lymphoreticular stromal cells can be non-autologous, or from a subject (source) different from the subject (source) of the hematopoietic cells (see column 27, lines 21-43, for example). Pykett et al disclose that lymphoreticular stromal cells can be obtained from lymphoid tissue and cryopreserved for later use (see column 14, lines 14-30, for example), which reads on the claimed cytotherapeutic unit wherein at least one type of cell is frozen separately from another type of cells (e.g. CD34+ cells) and wherein at least one of said cells has been characterized (i.e. is of lymphoid origin). In addition, Pykett discloses that unfractionated blood products can be retrieved from cryopreservative storage (see column 12, lines 50-53, for example). Pykett et al further teach that the entire matrix, lymphoreticular stromal cells and hematopoietic cells can be implanted into subjects (see column 2, lines 50-67, for example). As described above, Pykett et al teach an inventive embodiment comprising an implantable matrix with non-autologous stromal cells and hematopoietic cells obtained from a mixture of placenta and cord blood, which reads on a unit comprising cells of a plurality of different cell types obtained from different sources (e.g. lymphatic tissue and blood) wherein at least about one hundred cells are CD34+.

Claim 1 recites the limitations that "the contents of said unit being known with respect to the identities and numbers of at least some of said plurality" and "the unit being assayed to ensure the accuracy of said identities and numbers". Claim 2 is drawn to the limitation that the accuracy of the assay to determine the identities and numbers of at least some of the cells is certified. Claims 20-22 are drawn to the cytotherapeutic unit distributed with a certification of the contents of the unit, such as indication of cells excluded or absent from the unit. Claim 23 is drawn to the unit with certification that indicates how the contents of the unit render it suitable for therapy for an indicated disease or condition. These limitations appear to be drawn to knowledge concerning the cytotherapeutic unit, where in claim 1 the knowledge is the content or identity and numbers of the cells in the unit, and in claim 2 the knowledge is certification (e.g. assurance) that the assay is accurate. The identities and numbers of at least some of the cells in the cytotherapeutic unit is an inherent property of the unit. Whether the assay to determine the identities and numbers of the cells is accurate or not is an inherent property of the assay. Absence of particular cell types from a cytotherapeutic unit, whether deliberately excluded or not present to begin with, is an inherent property of the cytotherapeutic unit. In other words, certain cell types are present in the unit or they are not. Either the particular cytotherapeutic unit for an indicated disease state or condition is suitable based on the cell content or it is not suitable. Knowledge or certification of the excluded or absent cells does not alter the properties of the claimed cytotherapeutic unit. Likewise, certification of the suitability of the cytotherapeutic unit does not change the properties of the unit.

There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency); see also Toro Co. v. Deere & Co., 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention.") See MPEP 2112.

Therefore, the hematopoietic cell in the preparations taught by Pykett et al would have numbers and identities, and the assays performed by Pykett et al to determine numbers and viability would or would not be accurate. In order for the hematopoietic cell preparations taught by Pykett et al to anticipate the claimed cytotherapeutic unit, it is not necessary for the Pykett et al to have known the identities and numbers of at least some of the plurality of cells or to know or certify the accuracy of the assay. It is not necessary for the Pykett et al to specifically certify which cells are absent or have been excluded or whether the preparation of cells or matrix with cells is suitable for treating and immuno-compromised subject for the preparation to anticipate the claimed unit.

Claims 1-6, 8, 15-18, 20-23, 31-32, 34-35 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al (U.S Patent No. 5,677,139).

Johnson et al teach a population of cells comprising hematopoietic cells, including CD34+ cells, obtained from blood products. Johnson et al teach that the cells can be used for immune supplementation for a patient undergoing chemotherapy or radiation therapy (see column 9, lines 24-34, for example), which reads on a

cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells. Johnson et al teach embodiments wherein the hematopoietic cells are human pluripotent cells and may obtained from bone marrow, peripheral blood, umbilical cord blood, or peripheral blood mobilized stem cells (see column 5, lines 4-17).

Specifically, Johnson et al teach that five milliliters of venous blood were extracted from an umbilical cord prior to infant delivery. After delivery, the placenta was removed and blood contained in the placenta was collected. Johnson et al teach that the cord blood and placenta blood were mixed together before processing (see column 10, lines 24-34, in particular), which reads on cells from a plurality of sources and wherein one source is fetal cord blood or post-partum placenta. Johnson et al teach that the blood was centrifuged to separate mononuclear cells and then remaining erythrocytes were lysed, which reads on exclusion of at least one type of cell from the unit. The remaining number of viable cells was determined by trypan blue exclusion. Johnson et al teach that CD34+ cells were isolated using a CD34 progenitor cell selection system comprising mixing the cell sample with anti-human CD34 beads so that cells not bound to the paramagnetic beads could be aspirated away (see column 10, lines 53-67 and column 11, lines 1-32, for example). Johnson et al teach an embodiment in which CD34+ cells are co-cultured with thymic stromal cells at a concentration of 10^3 to 10^5 CD34+ cells per well for expansion and differentiation (see column 12, lines 19-32, for example). Subsequently, the identity of the cells was checked with type-specific antibodies in flow cytometry analysis (see column 12, lines 50-64, in particular), which reads on the contents of the unit being known with respect to

the numbers and identities of at least some of the plurality of cells, where the identities reflect the presence of absence of at least one antigenic determinant (e.g. CD34+), and also selection of the plurality of potent cells to render the unit suitable for therapy for an indicated disease. Antibodies specific for CD3, CD4 and CD8 were used to detect and characterize cells which were derived from the CD34+ population (see column 12, lines 49-67) which reads on a plurality of cells selected to render the unit suitable for therapy The cell preparation taught by Johnson et al reads on a cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells comprising cells obtained from umbilical cord blood and cell from a postpartum placenta wherein at least one type of cells have been removed from the unit (i.e. erythrocytes).

Since the culture taught by Johnson et al started with 10^3 to 10^5 CD34+ cells per well before expansion, absent evidence to the contrary, after harvest there would be at least about one hundred CD34+ cells. The cell preparation taught by Johnson et al is obtained by separating CD34+ cells from the blood products. One of skill in the art would recognize that blood contains many cell types (erythrocytes, granulocytes, agranulocytes and platelets). If CD34+ cells are separated from the original blood sample, than many or a plurality of cell types have been removed from the unit. Therefore, Johnson et al teach a cytotherapeutic unit comprising cells from a mixture of cord blood or postpartum placenta wherein a plurality of cells have been removed from the unit. The expanded and differentiated cell population containing and derived from CD34+ cells obtained from both cord blood and placental blood (i.e. two sources) taught by Johnson et al anticipates the claimed cytotherapeutic unit comprising a mixture of

cells obtained from cord blood and placenta, said cells comprising a plurality of different cell types (i.e. CD3, CD4, CD8 and CD34, at least one cell obtained from a source that differs from a source of another type.

Johnson et al disclose that lymphoreticular stromal cells can be obtained from lymphoid tissue and cryopreserved for later use (see column 12, lines 1-15, for example), which reads on the claimed cytotherapeutic unit wherein at least one type of cell is frozen separately from another type of cells (e.g. CD34+ cells) and wherein at least one of said cells has been characterized (i.e. is of thymic lymphoid origin).

As discussed above, limitations in claims 1-2 and 20-23 are drawn to knowledge concerning the cytotherapeutic unit, such as the content or identity and numbers of the cells in the unit, certification (e.g. assurance) that the assay is accurate or certification of the cell content of the unit. The identities and numbers of at least some of the cells in the cytotherapeutic unit is an inherent property of the unit. Whether the assay to determine the identities and numbers of the cells is accurate or not is an inherent property of the assay. Absence of particular cell types from a cytotherapeutic unit, whether deliberately excluded or not present to begin with, is an inherent property of the cytotherapeutic unit. In other words, certain cell types are present in the unit or they are not. Either the particular cytotherapeutic unit for an indicated disease state or condition is suitable based on the cell content or it is not suitable. Knowledge or certification of the excluded or absent cells does not alter the properties of the claimed cytotherapeutic unit. Likewise, certification of the suitability of the cytotherapeutic unit does not change the properties of the unit.

There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency); see also Toro Co. v. Deere & Co., 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention.") See MPEP 2112.

Therefore, the hematopoietic cells in the preparations taught by Johnson et al would have numbers and identities, and the assays performed by Johnson et al to determine numbers and viability would or would not be accurate. In order for the hematopoietic cell preparations taught by Johnson et al to anticipate the claimed cytotherapeutic unit, it is not necessary for the Johnson et al to have known the identities and numbers of at least some of the plurality of cells or to know or certify the accuracy of the assay. It is not necessary for the Johnson et al to specifically certify which cells are absent or have been excluded or whether the preparation of cells or matrix with cells is suitable for treating a subject for the preparation to anticipate the claimed unit.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pykett et al as applied to claim 1 herein above in view of Ende et al (Life Sciences 2001, of record).

Applicants claims a cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells comprising at least about one hundred CD34+ cells or at least about one hundred CD8+ cells within a plurality of potent cells, the contents of said unit being known with respect to the identities and numbers at least some of said plurality; the unit being assayed to ensure the accuracy of said identities and numbers and the unit comprising cells for a plurality of sources, wherein one source of said plurality of sources is fetal cord blood, fetal tissue, postpartum placenta or postpartum placenta perfusate and wherein the potent cells are obtained from at least two individuals.

As discussed in the above rejection, Pykett et al teach a population of cells comprising hematopoietic cells, including CD34+ cells, obtained from blood products. Pykett et al teach that the cells can be used to supplement or replenish a patient's hematopoietic progenitor cell population (see column 19, lines 12-25, for example), which reads on a cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells. Pykett et al teach embodiments wherein the hematopoietic cells may obtained from bone marrow, peripheral blood, umbilical cord blood, placental blood, fetal liver and lymphoid soft tissue (see column 3, lines 37-50). Pykett et al teach that mature differentiated cells can be selected against or CD34+ cells can be selected from the population of cells in the blood product by using paramagnetic anti-CD34 beads (see column 12, lines 31-50, for example). Pykett et al teach that five to ten

milliliters of blood were extracted from an umbilical cord prior to infant delivery. After delivery, the placenta was removed and blood contained in the placenta was collected. Pykett et al teach that the cord blood and placenta blood were mixed together before processing (see column 31, lines 10-25, in particular), which reads on cells from a plurality of sources and wherein one source is fetal cord blood or post-partum placenta.

Pykett et al teach that CD34+ cells were isolated using a CD34 progenitor cell selection system comprising mixing the cell sample with anti-human CD34 beads so that cells not bound to the paramagnetic beads could be aspirated away (see column 31, lines 10-40, for example). Pykett et al teach an embodiment in which five thousand CD34+ cells are co-cultured with thymic stromal cells and after 7 days, the CD34+ were harvested. Subsequently, the harvested cells were counted, assessed for viability and the presence of CD34 was checked using anti-CD34 antibodies in flow cytometry analysis (see column 33, lines 10-60, in particular), which reads on the contents of the unit being known with respect to the numbers and identities of at least some of the plurality of cells. Since the culture taught by Pykett et al started with five thousand CD34+ before expansion, absent evidence to the contrary, after harvest there would be at least about one hundred CD34+ cells.

Pykett et al does not teach the cytotherapeutic unit wherein the potent cells are obtained from at least two individuals or at least five individuals.

Ende et al teach a method of pooling umbilical cord samples before administration to marrow reconstitution after exposure to radiation. Ende et al discloses that a barrier to use of umbilical cord blood is that it is difficult to obtain enough stem

cells for effective grafting especially since adults require many more stem cells than children. Ende et al discloses an additional difficulty related to variability in the volume and quantity of cord blood samples (see page 1532, 1st paragraph, for example). Ende et al teach that fifteen human umbilical cord blood samples were obtained from full term neonates and that five milliliters of each were mixed in combination with two or three different other specimens (see page 1533, 2nd paragraph, for example). Ende et al teach that combined cord blood samples had an increase in percentage of colony forming units and a significant increase in the number of primitive colonies and CD34+ cells when compared to individual samples stored in the same manner (see page 1534, 3rd paragraph and Table 2, for example).

It would have been obvious to combine the teaching of Ende et al to use samples of cord blood from fifteen individuals with the hematopoietic cell composition of Pykett et al to make a cytotherapeutic unit wherein cells are obtained from at least two individuals or at least five individuals because Ende et al discloses that more cells can be obtained from multiple samples to provide adequate number of stem cells for therapy. The motivation to do so is the expected benefit of as suggested by Ende et al and Pykett et al being able to use cell from at least two or at least five different individuals to provide sufficient cells in therapeutic hematopoietic products for all patients, including adults or children of different ethnic origins. There is a reasonable expectation of success in using cells obtained from at least two individuals or at least five individuals because Ende et al teach that there is an increase in cell number after combination of samples and therapeutic hematopoietic products have worked previously as taught by Pykett et

al. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 1 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al as applied to claim 1 herein above in view of Ende et al (Life Sciences 2001, of record).

Applicants claims a cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells comprising a at least about one hundred CD34+ cells or at least about one hundred CD8+ cells within a plurality of potent cells, the contents of said unit being known with respect to the identities and numbers at least some of said plurality; the unit being assayed to ensure the accuracy of said identities and numbers and the unit comprising cells for a plurality of sources, wherein one source of said plurality of sources is fetal cord blood, fetal tissue, postpartum placenta or postpartum placenta perfusate and wherein the potent cells are obtained from at least two individuals.

As discussed in the above rejection, Johnson et al teach a population of cells comprising hematopoietic cells, including CD34+ cells, obtained from blood products. Johnson et al teach that the cells can be used for immune supplementation for a patient undergoing chemotherapy or radiation therapy (see column 9, lines 24-34, for example), which reads on a cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells. Johnson et al teach embodiments wherein the hematopoietic cells

are human pluripotent cells and may obtained from bone marrow, peripheral blood, umbilical cord blood, or peripheral blood stem cells (see column 5, lines 4-17).

Johnson et al teach that five milliliters of venous blood were extracted from an umbilical cord prior to infant delivery. After delivery, the placenta was removed and blood contained in the placenta was collected. Johnson et al teach that the cord blood and placenta blood were mixed together before processing (see column 10, lines 24-34, in particular), which reads on cells from a plurality of sources and wherein one source is fetal cord blood or post-partum placenta. The remaining number of viable cells was determined by trypan blue exclusion. Johnson et al teach that CD34+ cells were isolated using a CD34 progenitor cell selection system comprising mixing the cell sample with anti-human CD34 beads so that cells not bound to the paramagnetic beads could be aspirated away (see column 10, lines 53-67 and column 11, lines 1-32, for example). Johnson et al teach an embodiment in which CD34+ cells are co-cultured with thymic stromal cells at a concentration of 10^3 to 10^5 CD34+ cells per well for expansion and differentiation (see column 12, lines 19-32, for example). Subsequently, the identity of the cells was checked with type-specific antibodies in flow cytometry analysis (see column 12, lines 50-64, in particular), which reads on the contents of the unit being known with respect to the numbers and identities of at least some of the plurality of cells. Since the culture taught by Johnson et al started with 10^3 to 10^5 CD34+ cells per well before expansion, absent evidence to the contrary, after harvest there would be at least about one hundred CD34+ cells.

Johnson et al does not teach the cytotherapeutic unit wherein the potent cells are obtained from at least two individuals or at least five individuals.

Ende et al teach a method of pooling umbilical cord samples before administration to marrow reconstitution after exposure to radiation. Ende et al discloses that a barrier to use of umbilical cord blood is that it is difficult to obtain enough stem cells for effective grafting especially since adults require many more stem cells. Ende et al also discloses an additional difficulty related to variability in the volume and quantity of cord blood samples (see page 1532, 1st paragraph, for example). Ende et al teach that fifteen human umbilical cord blood samples were obtained from full term neonates and that five milliliters of each were mixed in combination with two or three different other specimens (see page 1533, 2nd paragraph, for example). Ende et al teach that combined cord blood samples had an increase in percentage of colony forming units and a significant increase in the number of primitive colonies and CD34+ cells when compared to individual samples stored in the same manner (see page 1534, 3rd paragraph and Table 2, for example).

It would have been obvious to combine the teaching of Ende et al to use samples of cord blood from two or more individuals with the hematopoietic cell composition of Johnson et al to make a cytotherapeutic unit wherein cells are obtained from at least two individuals or at least five individuals because Ende et al discloses that more cells can be obtained from multiple samples to provide adequate number of stem cells for therapy. The motivation to do so is the expected benefit of as suggested by Ende et al and Johnson et al being able to use cells from at least two individuals or at least five

individuals to provide sufficient cells in therapeutic hematopoietic products for all patients, including adults or children of different ethnic origins. There is a reasonable expectation of success in using cells obtained from at least two individuals or at least five individuals because Ende et al teach that there is an increase in cell number after combination of samples and therapeutic hematopoietic products have worked previously as taught by Johnson et al. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 34 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pykett et al as applied to claim 34 herein above in view of Woods et al (J. Hematother. Stem Cell Res. 2000, Vol. 9. Pages 161-173).

Applicants claims a cytotherapeutic unit in a frozen state suitable for treatment of a patient in need of hematopoietic cells comprising a mixture of cells obtained from umbilical cord cells and cells from a postpartum placenta, said cells comprising a plurality of different types, and at least one of the different types having been obtained from a source that differs from a source of another type and wherein at least about one hundred cells are CD34+ cells or at least about one hundred cells are CD8+.

As discussed above, Pykett et al teach a population of cells comprising hematopoietic cells, including CD34+ cells, obtained from blood products. Pykett et al teach that the cells can be used to supplement or replenish a patient's hematopoietic

progenitor cell population (see column 19, lines 12-25, for example), which reads on a cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells. Pykett et al teach embodiments wherein the hematopoietic cells are pluripotent or multipotent cells and may obtained from bone marrow, peripheral blood, umbilical cord blood, placental blood, fetal liver and lymphoid soft tissue (see column 3, lines 37-50). Pykett et al teach a method in which five to ten milliliters of blood were extracted from an umbilical cord prior to infant delivery and the placenta after delivery. One of skill in the art would recognized that blood contains many cell types (erythrocytes, granulocytes, agranulocytes and platelets). Pykett et al teach that cord blood and placenta blood were mixed together before processing (see column 31, lines 10-25, in particular), which reads on cells of a plurality of different types and at least one of the types being obtained from a source of another type. Pykett et al teach an embodiment in which five thousand CD34+ cells are co-cultured with thymic stromal cells and after 7 days, the CD34+ were harvested. Since the culture taught by Pykett et al started with five thousand CD34+ before expansion, absent evidence to the contrary, after harvest there would be at least about one hundred CD34+ cells. Pykett et al do not teach that the hematopoietic cell preparation is frozen.

Woods et al teach optimization of human placental/umbilical cord blood cryopreservation methods. Woods et al teach that cryopreservation of placental or cord blood derived hematopoietic cells, such as CD34+ cells, adds flexibility to methods of cord blood transplantation. Woods et al teach that cells from cord blood were first successfully cryopreserved over a decade ago. Woods et al teach a modification of the

preservation methods known in the art that uses a different cryoprotectant and found potential benefits in CD34+ preservation (see page 171, right column, 3rd paragraph, for example). Woods et al disclose that the ability to preserve relatively pure progenitor cell populations such as CD34+ cells would potentially minimize the total volume of a transplanted cell preparation and minimize dose dependent toxicity of cryoprotectants. Woods et al also disclose that the ability to store cryopreserved or frozen progenitor cells allows banking of cord blood and allowed time for necessary infectious disease screening and HLA typing. Woods et al disclose that freezing cord blood theoretically allows the preservation of cord-blood derived progenitor cells from at risk neonatal patients (see page 162, left column, 2nd paragraph).

It would have been obvious to one of skill in the art to combine the cryopreservation method as taught by Woods et al with the hematopoietic cell preparation taught by Pykett et al because Woods teach that it improves cord blood CD34+ preservation. The motivation to freeze the hematopoietic cell preparation is the expected benefit of being able to store the preparation for testing and typing of the cells and to store the cells when they are not going to be used immediately. The method of Woods et al preserves relatively pure population of specific potent cell types in minimal volumes with minimal amounts of cryoprotectant. There is reasonable expectation of success in freezing the hematopoietic cell preparation because it has worked previously in the cited techniques.

Claims 34 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Johnson et al as applied to claim 34 herein above in view of Woods et al (J. Hematother. Stem Cell Res. 2000, Vol. 9. Pages 161-173).

Applicants claims a cytotherapeutic unit in a frozen state suitable for treatment of a patient in need of hematopoietic cells comprising a mixture of cells obtained from umbilical cord cells and cells from a postpartum placenta, said cells comprising a plurality of different types, and at least one of the different types having been obtained from a source that differs from a source of another type and wherein at least about one hundred cells are CD34+ cells or at least about one hundred cells are CD8+.

Johnson et al teach a population of cells comprising hematopoietic cells, including CD34+ cells, obtained from blood products. Johnson et al teach that the cells can be used for immune supplementation for a patient undergoing chemotherapy or radiation therapy (see column 9, lines 24-34, for example), which reads on a cytotherapeutic unit suitable for treatment of a patient in need of hematopoietic cells. Johnson et al teach embodiments wherein the hematopoietic cells are human pluripotent cells and may obtained from bone marrow, peripheral blood, umbilical cord blood, or peripheral blood mobilized stem cells (see column 5, lines 4-17). Johnson et al teach that five milliliters of venous blood were extracted from an umbilical cord prior to infant delivery and extracted from the placenta after delivery. Johnson et al teach that the cord blood and placenta blood were mixed together before processing (see column 10, lines 24-34, in particular), which reads on cells of a plurality of different types and at least one of the types being obtained from a source of another type.

Johnson et al teach an embodiment in which CD34+ cells are selected from the sample and are co-cultured with thymic stromal cells at a concentration of 10^3 to 10^5 CD34+ cells per well for expansion and differentiation (see column 12, lines 19-32, for example). Since the culture taught by Johnson et al started with 10^3 to 10^5 CD34+ cells per well before expansion, absent evidence to the contrary, after harvest there would be at least about one hundred CD34+ cells. Johnson et al do not teach that the hematopoietic cell preparation is frozen.

Woods et al teach optimization of human placental/umbilical cord blood cryopreservation methods. Woods et al teach that cryopreservation of placental or cord blood derived hematopoietic cells, such as CD34+ cells, adds flexibility to methods of cord blood transplantation. Woods et al teach that cells from cord blood were first successfully cryopreserved over a decade ago. Woods et al teach a modification of the preservation methods known in the art that uses a different cryoprotectant and found potential benefits in CD34+ preservation (see page 171, right column, 3rd paragraph, for example). Woods et al disclose that the ability to preserve relatively pure progenitor cell populations such as CD34+ cells would potentially minimize the total volume of a transplanted cell preparation and minimize dose dependent toxicity of cryoprotectants. Woods et al also disclose that the ability to store cryopreserved or frozen progenitor cells allows banking of cord blood and allowed time for necessary infectious disease screening and HLA typing. Woods et al disclose that freezing cord blood theoretically allows the preservation of cord-blood derived progenitor cells from at risk neonatal patients (see page 162, left column, 2nd paragraph).

It would have been obvious to one of skill in the art to combine the cryopreservation method as taught by Woods et al with the hematopoietic cell preparation taught by Pykett et al because Woods teach that it improves cord blood CD34+ preservation. The motivation to freeze the hematopoietic cell preparation is the expected benefit of being able to store the preparation for testing and typing of the cells and to store the cells when they are not going to be used immediately. The method of Woods et al preserves relatively pure population of specific potent cell types in minimal volumes with minimal amounts of cryoprotectant. There is reasonable expectation of success in freezing the hematopoietic cell preparation because it has worked previously in the cited techniques.

Conclusion

Claims 1-6, 8-9, 12-13, 15-18, 20-23, 31-32, 34-37 and 50 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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6/9/2006

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